

## A Cellular Model of Angiogenesis

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Angiogenesis, the formation of new blood vessels, is an important step in modelling tumor growth. When angiogenesis occurs inside a tumor, the newly acquired vasculature provides an abundant source of nutrients to the tumor and increases the tumor's capacity to export waste products, thereby allowing the tumor to sustain continued growth unattainable by avascular tumors. Furthermore, tumor vascularization has been closely linked to metastasis [1], a progressive stage of cancer often indicative of a poor prognosis. A reliable model of tumor angiogenesis will be useful in answering questions related to how a tumor grows once angiogenesis has developed and to allow for the testing of new anti-angiogenic drug therapies.

To ensure its sustained growth, a tumor may secrete tumor angiogenic factor (TAF), a chemical compound which causes nearby capillaries to form sprouts which migrate towards the tumor. Two such chemical compounds which have been found to be important in tumor growth are proteins called vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) [3]. Endothelial cells, which form the lining of neighboring blood vessels, respond to this chemotactic stimulus by degrading the vessel membrane, proliferating and migrating towards the chemical source.

Our model is a hybrid of cellular dynamics, which are modelled using a lattice Monte Carlo model, and reaction-diffusion dynamics of angiogenic growth factor, which are represented by PDEs. We allow endothelial cells, which are embedded in a medium composed of normal cells and extracellular matrix, to respond to a chemical gradient of TAF and migrate towards the chemical source. We wish to investigate the effects of 3 different types of chemical source pro-

files: 1) a point source, 2) a line source, and 3) a parabolic source, to determine which source profile most closely resembles actual blood vessel growth nearby and within a real tumor.

Future work will be to extend our 2-D model of angiogenesis to three dimensions, where we can then integrate this model with an existing 3-D model of avascular tumor growth [2]. The result would be a model that takes us through avascular tumor growth, the initiation and development of angiogenesis, and then into vascular tumor growth, providing a more complete simulation of the growth of a tumor.

## References

- [1] Ellis, L., Fiddler, I., Angiogenesis and Breast Cancer Metastasis, *Lancet*, **346** (1995) 488–9.
- [2] Jiang, Y., Pjesivac-Grbovic, J., Freyer, J. P., Cantrell, C., A Multiscale Model for Avascular Tumor Growth, preprint.
- [3] National Cancer Institute. Science Behind the News. Understanding Angiogenesis